Information for Healthcare Professionals

Natalizumab (Tysabri)

- **FDA ALERT [02/2006]: The FDA has lifted the clinical hold on Biogen-IDEC's trials of natalizumab for patients with multiple sclerosis (MS). Biogen-IDEC can now resume administration of natalizumab to patients with relapsing-remitting MS who had previously been treated with the drug in clinical trials. Biogen-IDEC had previously suspended marketing of natalizumab and all further dosing of patients in on-going clinical trials. This decision was made after confirmation of one fatal case and one additional case of severely disabling progressive multifocal leukoencephalopathy (PML) in patients receiving natalizumab for MS. A third case of PML, this one fatal, in a patient with Crohn's Disease had been identified shortly thereafter.**

- **FDA has since received detailed information from Biogen-IDEC about the condition of all available patients who had received natalizumab in clinical studies under an IND. No additional cases of PML were identified. In addition, Biogen will be monitoring patients very closely for PML when studies resume. While FDA remains very concerned about the potential for PML associated with natalizumab use, existing data suggest that natalizumab may be effective against MS, which is a devastating neurologic disease. FDA has decided to allow studies to resume under IND to obtain more information that may permit us to understand the true degree of risk and/or benefit from natalizumab.**

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program using the contact information at the bottom of this sheet.

Considerations

- Physicians, and their patients who had previously been receiving natalizumab within an IND study at the time of the suspension of use, should discuss with a study physician the potential risks and potential benefits of resuming treatment with natalizumab.

- Physicians and their patients must fully understand the requirements of the new monitoring programs.

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Data Summary

At the time of its approval, approximately 1,100 patients with MS had received natalizumab for a period of one year or more. No cases of PML were observed during the clinical trials performed prior to approval of natalizumab. Later, the FDA received two reports from Biogen-IDEC of PML in patients receiving natalizumab in clinical trials of MS. One other case of PML, in a patient with Crohn's Disease, was identified shortly thereafter.

PML is a serious, progressive neurologic disorder caused by infection of the central nervous system by JC virus, a member of the papovavirus family. JC virus is carried in a latent form by 70-75% of the general population but generally does not cause symptoms. PML is rare, but when it occurs it frequently results in irreversible neurologic deterioration and death, and there is no known effective treatment for the disease.